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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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09/112,041 07/08/98 GHETIE

M UTSD: 521/WIM

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EXAMINER

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HUNT, J

ART UNIT

PAPER NUMBER

1642

DATE MAILED:

03/30/01 *JH*

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

| | |
|--------------------------------------|--------------------------------------|
| Application No. 09/112,041 | Applicant(s) Ghetie et al. |
| Examiner Jennifer Hunt | Group Art Unit 1642 |



THE PERIOD FOR RESPONSE: [check only a) or b)]

- a) expires _____ months from the mailing date of the final rejection.
- b) expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

Appellant's Brief is due two months from the date of the Notice of Appeal filed on Feb 15, 2001 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Oct 12, 2000 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

The proposed amendment(s):

- will be entered upon filing of a Notice of Appeal and an Appeal Brief.
- will not be entered because:
 - they raise new issues that would require further consideration and/or search. (See note below).
 - they raise the issue of new matter. (See note below).
 - they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
 - they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

Applicant's response has overcome the following rejection(s):

Applicant's amendment and arguments overcome the rejections under 35 USC 102(b) only.

- Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.
- The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.
- The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
- For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):
 - Claims allowed: _____
 - Claims objected to: _____
 - Claims rejected: 1, 4, 5, 7-9, 11, 16, 17, 21-23, 25, 43, 46, 47, and 49-51
- The proposed drawing correction filed on _____ has has not been approved by the Examiner.
- Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____.
- Other

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Attachment to Advisory Action

Claim Rejections Withdrawn

1. The grounds of rejection of claims 1-7, 11-21, 25, 43-49, and 52 under 35 U.S.C. 102(b) as being anticipated by *Ahlem et al., US Patent 5,273,743, December 28, 1993* is withdrawn in light of applicant's arguments and amendments thereto.
2. The grounds of rejection of claims 1-2, 6-7, 11-12, 21, 23, and 49 under 35 U.S.C. 102(b) as being anticipated by *Cumber et al., The Journal of Immunology* is withdrawn in light of applicant's arguments and amendments thereto.

Claim Rejections Maintained

3. The rejection of claims 1, 3, 9, 11, 13, and 23 under 35 U.S.C. 102(e) as being anticipated by *Bagshawe et al., US Patent 5,683,694, November 4, 1997* is maintained for reasons of record.

Applicant argues that the conjugate of Bagshawe is different from the instantly claimed invention because the conjugate of the instantly claimed invention exhibits anti-neoplastic activity, and the conjugate of Bagshawe fails to exhibit anti-neoplastic activity because it relies on the cytotoxic agent to exhibit that activity. Applicant then adds that the instantly claimed homoconjugates "were surprisingly found to be capable of causing target cells to undergo cell cycle arrest and/or apoptosis initiated by negative signaling resulting from binding and hypercrosslinking of cell surface antigens to the homoconjugate".

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Applicant's arguments filed 2-20-2001 have been fully considered but they are not persuasive.

Bagshawe teaches a conjugate comprising two portions, both of which can be monoclonal antibodies, thus a homoconjugate of two monoclonal antibodies. The second portion, which can be a monoclonal antibody, exerts cytotoxic activity (including anti-tumor activity). Thus the conjugate does exert the anti-neoplastic activity. Further, the limitations argued by applicant (that the antibodies themselves exert the anti-neoplastic activity) are not instantly claimed. Anything which is a part of the conjugate could exert anti-neoplastic activity and still anticipate the claim.

Further, with regard to applicant's description of the surprising discoveries about the instantly claimed homoconjugates, these properties are not instantly claimed and thus applicant's arguments are not commensurate in scope with the claims.

4. The rejection of claims 1-3, 6-15, 18-25, 43-45, and 48-51 under 35 U.S.C. 103(a) as being unpatentable over *Glennie, WO 91/03493, March 21, 1991, Ghetie et al., Exp. Opin. Invest. Drugs, Vol 5, No 3, pages 309-321, or Bosslet et al., US Patent 5,591,828, January 7, 1997* in view of Wolff et al., WO 92/04053 is maintained for reasons of record.

Applicant argues that Glennie, Ghetie et al., and Bosslet et al. all teach away from or fail to teach homoconjugates, and thus Wolff et al. cannot properly be combined with the cited references.

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Applicant's arguments filed 2-20-2001 have been fully considered but they are not persuasive.

As set forth in the previous office action, Glennie, Ghetie et al., and Bosslet et al. each teach a conjugate of antibodies which do not comprise Fc regions. Glennie, Ghetie et al., and Bosslet et al. each teach the desirability of antibody conjugates, as having greater binding activity and greater response than normal antibodies. Further, they each teach the desirability of removal of the Fc region of the antibodies of the conjugates, for reasons of tumor penetration and decreased non-specific immune response.

The references Glennie, Ghetie et al., and Bosslet et al. do not teach homoconjugates, however, they also do not teach away from homoconjugates, as applicant has argued. The references all teach heteroconjugate antibodies as exemplified embodiments, however they do not teach that there would be any reason not to construct homoconjugates of the same general structure. The citations which applicant points to for support of the argument that the references teach away from homoconjugates are merely examples of heteroconjugates. No where in any of the references is there a suggestion that homoconjugates would not function as effectively, or that homoconjugates would not enjoy the same advantages of the taught heteroconjugates.

Further, the teaching of motivation to make homoconjugates is supplied by Wolff et al., which teaches the desirability of homoconjugate antibodies as having greater binding activity and greater response than normal antibodies.

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Thus all of the references are drawn to antibody conjugates which provide advantages over traditional antibodies for the purpose of therapeutic administration. Drawing from this fact, "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to form the third composition that is to be used for the very same purpose: idea of combining them flows logically from their having been taught individually in the prior art." In re Kerkhoven (205 USPQ 1069, CCPA 1980). It is well known in the art as set forth above that antibody conjugates without Fc regions, and homoconjugates of antibodies are both useful for inhibiting the growth of tumors. Thus it would have *been prima facie* obvious to combine the teachings of Glennie, Ghetie et al., and Bosslet et al. and Wolff et al., for the purposes of creating a more effective conjugate for therapy.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

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Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Hunt

March 28, 2001


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